

## **REMARKS**

### **I. Status of the Claims**

Claims 1, 3-9, and 11-13 were pending at the time of the Office Action. Claims 1 and 13 have been amended. No claims have been cancelled or added. Therefore, claims 1, 3-9, and 11-13 remain pending.

### **II. Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claims 1, 3-9, and 11-12 stand rejected as being indefinite under the second paragraph of 35 U.S.C. § 112. Claim 1 has been amended to address the Examiner's concerns. Claim 13 has been amended similarly. Disclosure supporting these amendments may be found at least at the paragraph beginning at page 9, line 21 of the originally filed application. Reconsideration and withdrawal of the rejections are respectfully requested.

### **III. Rejections Under 35 U.S.C. § 103**

To establish prima facie obviousness of a claimed invention, all the claim limitations must be shown by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). Because all proposed combinations fail to teach every claim limitation, Applicants respectfully submit that the present rejections are improper.

#### **A. Claims 1, 3-6, 8-9, and 11-13 Are Patentable Over Wu In View of Shaffer and Cole**

Claims 1, 3-6, 8-9, and 11-13 stand rejected as being unpatentable over Wu in view of Shaffer, and further in view of Cole. Applicants respectfully traverse.

Claims 1 and 13 each recite the limitation "wherein identifying the plurality of differentially expressed genes comprises utilizing a paired T-test and an associative T-test." Claims 3-6, 8-9, and 11-12 each depend from either claim 1 or claim 13, and therefore also contain the limitation.

The Office Action asserts that the “[a]s defined in the specification at p. 13, lines 10-11, an ‘associative T-test’ is a standard T-test applied to the comparison of expression deviations. The ‘associative T-test’ as defined in specification is also known in the art as an F-test.” Office Action at 5. Applicants respectfully submit that this assertion is incorrect.

The “associative T-test” defined in the specification is different than what is known in the art as an F-test. As known in the art, an F-test is an analysis of variance that may include comparison of standard deviations of two or more populations (e.g., comparison of the standard deviation of a first population to the standard deviation of a second population). It appears that the assertion of the Office Action may be based on a misreading of the phrase “comparison of expression deviations.” These “expression deviations” of members of a group are not the same as a “standard deviation” calculated for that group.

Consideration of the entirety of the paragraph containing the two sentences cited in the Office Action clarifies that the associative T-test may be a comparison between residuals (e.g., expression deviations from a reference value, such as a regression line) of, for example, the members of a reference group and a control group:

It is possible to substitute the typical paired comparison of gene expressions between control and experimental groups with the comparison of their residuals. In this analysis it is determined if a given gene of the experimental group belongs to (or can be associated with) the reference group. Denoted an associative T test, it is actually a standard Student T-test applied to the comparison of expression deviations. An associative T-test dramatically increases the power of comparisons relative to a paired T-test. In the data analyzed here, this is due to the fact that eight replicates from the control group are compared with several hundred values of the reference group. As a result, a large number of positive determinations can be obtained with stringent thresholds (**FIG. 4D**).

Application at 13 (emphasis added). The Application provides additional description of an associative T-test that includes a comparison of residuals from one group with residuals from a second group:

(c) An associative T-test in which the replicated residuals for each gene of the experimental group are compared with the entire set of residuals from the reference group defined earlier. The null hypothesis is checked to determine if gene expression in the experimental group is associated with the reference group defined above. The significance threshold is corrected to make improbable the appearance of false positive determinations.

Application at 11 (emphasis added). Furthermore, the Summary describes:

The associative T-test can include a test in which a plurality of replicated residuals for each gene of the plurality of the expression profiles of the experimental group are compared with an entire set of residuals from the plurality of expression profiles of the control group.

Application at 6. Therefore, the “associative T-test” defined in specification, in which residuals of gene expressions members of a group (e.g., expression deviations) may be compared, differs from the analysis of variance known in the art as an F-test, in which the standard deviations of two or more groups are compared. Accordingly, the limitation “wherein identifying the plurality of differentially expressed genes comprises utilizing a paired T-test and an associative T-test” is not disclosed or suggested by any of the Wu, Shaffer, or Cole references, and for at least this reason the rejection should be withdrawn.

**B. Claims 1 and 7 Are Patentable Over Wu In View of Shaffer, Cole, and Jensen**

Claims 1 and 7 stand rejected as being unpatentable over Wu in view of Shaffer, and in view of Cole, and further in view of Jensen. Applicants respectfully traverse.

As discussed above, the combination of Wu in view of Shaffer, and in view of Cole fails to disclose or suggest “wherein identifying the plurality of differentially expressed genes comprises utilizing a paired T-test and an associative T-test,” as recited in claim 1. Jensen does not cure this deficiency. Therefore, Applicants respectfully submit that the cited references fail to teach or suggest in their entirety, all of the elements of claims 1.

Claim 7 depends from claim 1, and therefore contains all elements recited by claim 1. Accordingly, the cited references fail to teach or suggest in their entirety, all of the elements of claims 7.

For at least these reasons, withdrawal of the rejection is respectfully requested.

### CONCLUSION

Applicants believe that these remarks fully respond to all outstanding matters for this application, and respectfully submit that all claims are in condition for allowance. Should the Examiner have any questions regarding this submission, a telephone call to the undersigned agent at 512-536-3027 is invited.

Respectfully submitted,

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